

(19) World Intellectual Property
Organization
International Bureau



P03/186-82

(43) International Publication Date
6 May 2005 (06.05.2005)

PCT

(10) International Publication Number
WO 2005/039547 A1

(51) International Patent Classification⁷: **A61K 31/00**,
A61P 1/16, C07D 417/14, 213/74

(DE). JONCZYK, Alfred [DE/DE]; Schepp Allee 57,
64295 Darmstadt (DE).

(21) International Application Number:
PCT/EP2004/010396

(74) Common Representative: **MERCK PATENT GMBH**;
Frankfurter Strasse 250, 64293 Darmstadt (DE).

(22) International Filing Date:
16 September 2004 (16.09.2004)

(81) Designated States (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
03022048.7 1 October 2003 (01.10.2003) EP

(71) Applicant (*for all designated States except US*): **MERCK
PATENT GMBH** [DE/DE]; Frankfurter Strasse 250,
64293 Darmstadt (DE).

(84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **GOODMAN**,
Simon [DE/DE]; Friedrich-Ebert Strasse 102a, 64347
Griesheim (DE). **SCHUPPAN**, Dettlef [DE/DE]; Baumzeil
2, 91088 Bubenreuth (DE). **PATSENKER**, Eleonora
[BY/DE]; Vierzigmannstrasse 17/30, 91054 Erlangen
(DE). **POPOV**, Yury [BY/DE]; Woehrstrasse 1, 91054
Erlangen (DE). **BAUER**, Michael [DE/DE]; Mozart-
strasse 54b, 91052 Erlangen (DE). **WIESNER**, Matthias
[DE/DE]; Beethovenring 10, 64342 Seeheim-Jugenheim

Published:

— with international search report

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: ALFAVBETA3 AND ALFAVBETA6 INTEGRIN ANTAGONISTS AS ANTIFIBROTIC AGENTS

(57) Abstract: This invention relates to inhibition of α v integrins, especially α v β 3 and α v β 6 integrins, by specific antagonists, preferably non-peptidic antagonists, related compounds and compounds with comparable specificity, that downregulate fibrogenesis by inhibiting cell migration and production of pro-fibrogenic molecules (e.g., collagens, TIMP-1) and cytokines (e.g., CTGF) by activated hepatic stellate cells/myofibroblasts, activated epithelia and endothelia. These antagonists alone or in combination with other agents can effectively prevent, mitigate or even reverse development of advanced fibrosis, such as fibrosis/cirrhosis of the liver and fibrosis of other organs, such as lungs, kidneys, intestine, pancreas, skin and arteries.

WO 2005/039547 A1